

IN THE SPECIFICATION

Please amend the specification as follows:

[0001] This application claims priority to Austrian application A 1872/98, filed November 10, 1998 and PCT application PCT/AT99/00272, filed November 10, 1999 ~~W000/28021~~, published May 18, 2000, hereby incorporated in their entirety by this reference.

[0061] Modified Factor VIII is preferably produced by recombinant expression. It may be produced recombinantly by means of any usual expression system such as, but not limited to, permanent cell lines or viral expression systems. Permanent cell lines are produced by the stable integration of foreign DNA into the host cell genome of, for instance, vero, MRC5, CHO (Chinese Hamster Ovary), BHK (baby hamster kidney), 293, Sk-Hep1 cells, in particular hepatic and renal cells, fibroblasts, keratinocytes or myoblasts, hepatocytes or stem cells, hematopoietic stem cells, or by an episomal vector derived, for instance, from papilloma virus. Virus expression systems such as vaccinia virus, baculovirus or retrovirus systems may likewise be used. Generally, vero, MRC5, CHO, BHK, 293, Sk-Hep1, glandular, hepatic and renal cells are used as cell lines. Eukaryotic expression systems that may be used include yeast cells, endogenous glandular cells (e.g., glands of transgenic animals) and also other types of cells. Naturally, transgenic animals may also be used for the expression of the polypeptides of the present invention or derivatives thereof. CHO-DHFR cells have proved to be particularly suitable for the expression of recombinant proteins (Urlaub et al., Proc. Natl. Acad. Sci., U.S.A., Vol. 77, pp. 4216-4220, 1980).

[0063] The Factor VIII polypeptide of the present invention is expressed in the respective expression system under the control of a suitable promoter. Any of the known promoters such as SV40, CMV (cytomegalovirus), RSV (respiratory syncytial virus), HSV (herpes simplex virus), EBV (Epstein Barr virus), p-actin, hGH (human growth hormone) or inducible promoters such as, e.g., hsp or metallothionein promoter are suitable for eukaryotes expression.

[0070] The data were analyzed by means of Biacore Evaluation Software (Pharmacia Biosensor AB, Uppsala, Sweden). The data analysis demonstrated that the interaction between the light chain of Factor VIII corresponded best with two classes of binding sites. The association and dissociation speed rate constants (k_{on} and k_{off} , respectively) were calculated for the two binding sites. These speed constants were subsequently used to obtain the affinity equilibrium constants (K_d) for these interactions.